

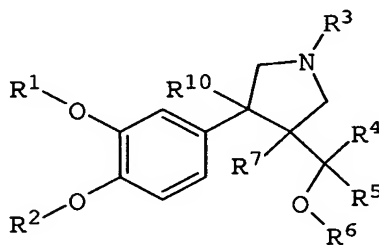
IN THE CLAIMS:

1-53. (Cancelled)

54. (Cancelled)

55. (Cancelled)

56. (Currently amended) A method of treating a mammal ~~having a condition where inhibition of a~~
~~cAMP specific PDE is of a therapeutic benefit for~~
rheumatoid arthritis, osteoarthritis, gouty arthritis,
or spondylitis comprising administering to said mammal an effective amount of a pharmaceutical composition comprising of (a) a compound of



wherein R¹ is selected from the group consisting of hydrogen, lower alkyl, bridged alkyl, aryl, cycloalkyl, a 4-, 5-, or 6-membered saturated heterocycle, heteroaryl, C₁₋₄alkylenearyl, C₁₋₄alkyleneOaryl, C₁₋₄alkyleneheteroaryl, C₁₋₄alkyleneHet, C₂₋₄alkylenearyl-Oaryl, C₁₋₄alkylene bridged alkyl, C₁₋₄alkylenecycloalkyl, substituted or unsubstituted propargyl, substituted or unsubstituted allyl, and halocycloalkyl;

R² is selected from the group consisting of hydrogen, methyl, and halo-substituted methyl;

R^3 is selected from the group consisting of $C(=O)OR^7$, $C(=O)R^7$, $NHC(=O)OR^7$, $C_{1-3}alkyleneC(=O)OR^8$, $C_{1-3}alkyleneC(=O)R^8$, $C(=NH)NR^8R^9$, $C(=O)NR^8R^9$, $C(=O)C(=O)NR^8R^9$, $C(=O)C(=O)OR^8$, $C_{1-4}alkyleneOR^8$, aryl, $C_{1-3}alkylene-aryl$, $C_{1-3}alkyleneheteroaryl$, $SO_2heteroaryl$, Het, and heteroaryl;

R^4 is selected from the group consisting of hydrogen, lower alkyl, haloalkyl, cycloalkyl, and aryl;

R^5 is selected from the group consisting of hydrogen, lower alkyl, alkynyl, haloalkyl, hydroxyalkyl, cycloalkyl, and aryl;

R^6 is selected from the group consisting of hydrogen, lower alkyl, and $C(=O)R^7$;

R^7 is selected from the group consisting of lower alkyl, branched or unbranched, $C_{1-4}alkylenearyl$, cycloalkyl, Het, $C_{1-4}alkylenecycloalkyl$, heteroaryl, and aryl, each optionally substituted with one or more of $OC(=O)R^8$, $C(=O)OR^8$, OR^8 , NR^8R^9 , or SR^8 ;

R^8 and R^9 , same or different, are selected from the group consisting of hydrogen, lower alkyl, cycloalkyl, aryl, heteroaryl, $C(=O)Oalkyl$, $C(=O)Oaryl$, $C(=O)alkyl$, $alkylSO_2$, $haloalkylSO_2$, $C(=O)C_{1-3}alkylene-aryl$, $C(=O)OC_{1-4}alkylenearyl$, $C_{1-4}alkylenearyl$, and Het, or R^8 and R^9 together form a 4-membered to 7-membered ring;

R^{10} is selected from the group consisting of hydrogen, alkyl, haloalkyl, cycloalkyl, aryl, $C(=O)-alkyl$, $C(=O)cycloalkyl$, $C(=O)aryl$, $C(=O)Oalkyl$, $C(=O)-Ocycloalkyl$, $C(=O)aryl$, CH_2OH , $CH_2Oalkyl$, CHO , CN , NO_2 , and SO_2R^{11} ;

R^{11} is selected from the group consisting of alkyl, cycloalkyl, trifluoromethyl, aryl, aralkyl, and NR^8R^9 ; or a salt or solvate thereof; and

(b) a pharmaceutically acceptable carrier.

57. (Cancelled)

58. (Cancelled)

59. (Cancelled)

60. (Cancelled)

61. (Cancelled)

62. (Cancelled)

63. (Cancelled)

64. (Cancelled)

65. (Cancelled)

66. (Cancelled)

67. (Cancelled)

68. (Cancelled)

69. (Cancelled)

70. (Cancelled)

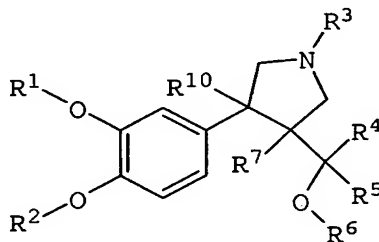
71. (Cancelled)

72. (Cancelled)

73. (Cancelled)

74. (Cancelled)

75. (New) A method of treating a mammal for thyroid-associated ophthalmopathy, Behcet disease, sepsis, septic shock, endotoxic shock, gram negative sepsis, gram positive sepsis, toxic shock syndrome, allergic conjunctivitis, vernal conjunctivitis, or eosinophilic granuloma comprising administering to said mammal an effective amount of a pharmaceutical composition comprising (a) a compound having a formula



wherein R¹ is selected from the group consisting of hydrogen, lower alkyl, bridged alkyl, aryl, cycloalkyl, a 4-, 5-, or 6-membered saturated heterocycle, heteroaryl, C₁₋₄alkylenearyl, C₁₋₄alkyleneOaryl, C₁₋₄alkyleneheteroaryl, C₁₋₄alkyleneHet, C₂₋₄alkylenearyl-Oaryl, C₁₋₄alkylene bridged alkyl, C₁₋₄alkylenecycloalkyl, substituted or unsubstituted propargyl, substituted or unsubstituted allyl, and halocycloalkyl;

R² is selected from the group consisting of hydrogen, methyl, and halo-substituted methyl;

R^3 is selected from the group consisting of $C(=O)OR^7$, $C(=O)R^7$, $NHC(=O)OR^7$, $C_{1-3}alkyleneC(=O)OR^8$, $C_{1-3}alkyleneC(=O)R^8$, $C(=NH)NR^8R^9$, $C(=O)NR^8R^9$, $C(=O)C(=O)NR^8R^9$, $C(=O)C(=O)OR^8$, $C_{1-4}alkyleneOR^8$, aryl, $C_{1-3}alkylene$ -aryl, $C_{1-3}alkyleneheteroaryl$, $SO_2heteroaryl$, Het, and heteroaryl;

R^4 is selected from the group consisting of hydrogen, lower alkyl, haloalkyl, cycloalkyl, and aryl;

R^5 is selected from the group consisting of hydrogen, lower alkyl, alkynyl, haloalkyl, hydroxyalkyl, cycloalkyl, and aryl;

R^6 is selected from the group consisting of hydrogen, lower alkyl, and $C(=O)R^7$;

R^7 is selected from the group consisting of lower alkyl, branched or unbranched, $C_{1-4}alkylenearyl$, cycloalkyl, Het, $C_{1-4}alkylenecycloalkyl$, heteroaryl, and aryl, each optionally substituted with one or more of $OC(=O)R^8$, $C(=O)OR^8$, OR^8 , NR^8R^9 , or SR^8 ;

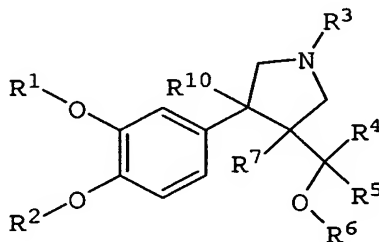
R^8 and R^9 , same or different, are selected from the group consisting of hydrogen, lower alkyl, cycloalkyl, aryl, heteroaryl, $C(=O)Oalkyl$, $C(=O)Oaryl$, $C(=O)alkyl$, $alkylSO_2$, $haloalkylSO_2$, $C(=O)C_{1-3}alkylene$ -aryl, $C(=O)OC_{1-4}alkylenearyl$, $C_{1-4}alkylenearyl$, and Het, or R^8 and R^9 together form a 4-membered to 7-membered ring;

R^{10} is selected from the group consisting of hydrogen, alkyl, haloalkyl, cycloalkyl, aryl, $C(=O)$ -alkyl, $C(=O)cycloalkyl$, $C(=O)aryl$, $C(=O)Oalkyl$, $C(=O)O$ -cycloalkyl, $C(=O)aryl$, CH_2OH , $CH_2Oalkyl$, CHO , CN , NO_2 , and SO_2R^{11} ;

R^{11} is selected from the group consisting of alkyl, cycloalkyl, trifluoromethyl, aryl, aralkyl, and NR^8R^9 ; or a salt or solvate thereof; and

(b) a pharmaceutically acceptable carrier.

76. (New) A method of treating a mammal for thyroid-associated ophthalmopathy, Behcet disease, asthma, chronic bronchitis, allergic rhinitis, adult respiratory distress syndrome, chronic pulmonary inflammatory disease, chronic obstructive pulmonary disease, silicosis, or pulmonary sarcoidosis comprising administering to said mammal an effective amount of a pharmaceutical composition comprising (a) a compound having a formula



wherein R^1 is selected from the group consisting of hydrogen, lower alkyl, bridged alkyl, aryl, cycloalkyl, a 4-, 5-, or 6-membered saturated heterocycle, heteroaryl, C_{1-4} alkylenearyl, C_{1-4} alkyleneOaryl, C_{1-4} alkyleneheteroaryl, C_{1-4} alkyleneHet, C_{2-4} alkylenearyl-Oaryl, C_{1-4} alkylene bridged alkyl, C_{1-4} alkylenecycloalkyl, substituted or unsubstituted propargyl, substituted or unsubstituted allyl, and halocycloalkyl;

R^2 is selected from the group consisting of hydrogen, methyl, and halo-substituted methyl;

R^3 is selected from the group consisting of $C(=O)OR^7$, $C(=O)R^7$, $NHC(=O)OR^7$, $C_{1-3}alkyleneC(=O)OR^8$, $C_{1-3}alkyleneC(=O)R^8$, $C(=NH)NR^8R^9$, $C(=O)NR^8R^9$, $C(=O)C(=O)NR^8R^9$, $C(=O)C(=O)OR^8$, $C_{1-4}alkyleneOR^8$, aryl, $C_{1-3}alkylene-aryl$, $C_{1-3}alkyleneheteroaryl$, $SO_2heteroaryl$, Het, and heteroaryl;

R^4 is selected from the group consisting of hydrogen, lower alkyl, haloalkyl, cycloalkyl, and aryl;

R^5 is selected from the group consisting of hydrogen, lower alkyl, alkynyl, haloalkyl, hydroxyalkyl, cycloalkyl, and aryl;

R^6 is selected from the group consisting of hydrogen, lower alkyl, and $C(=O)R^7$;

R^7 is selected from the group consisting of lower alkyl, branched or unbranched, $C_{1-4}alkylenearyl$, cycloalkyl, Het, $C_{1-4}alkylenecycloalkyl$, heteroaryl, and aryl, each optionally substituted with one or more of $OC(=O)R^8$, $C(=O)OR^8$, OR^8 , NR^8R^9 , or SR^8 ;

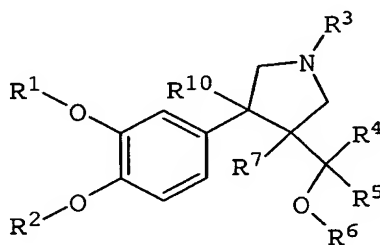
R^8 and R^9 , same or different, are selected from the group consisting of hydrogen, lower alkyl, cycloalkyl, aryl, heteroaryl, $C(=O)Oalkyl$, $C(=O)Oaryl$, $C(=O)alkyl$, $alkylSO_2$, $haloalkylSO_2$, $C(=O)C_{1-3}alkylene-aryl$, $C(=O)OC_{1-4}alkylenearyl$, $C_{1-4}alkylenearyl$, and Het, or R^8 and R^9 together form a 4-membered to 7-membered ring;

R^{10} is selected from the group consisting of hydrogen, alkyl, haloalkyl, cycloalkyl, aryl, $C(=O)-alkyl$, $C(=O)cycloalkyl$, $C(=O)aryl$, $C(=O)Oalkyl$, $C(=O)-Ocycloalkyl$, $C(=O)aryl$, CH_2OH , $CH_2Oalkyl$, CHO , CN , NO_2 , and SO_2R^{11} ;

R^{11} is selected from the group consisting of alkyl, cycloalkyl, trifluoromethyl, aryl, aralkyl, and NR^8R^9 ; or a salt or solvate thereof; and

(b) a pharmaceutically acceptable carrier.

77. (New) A method of treating a mammal for reperfusion injury of the myocardium, brain, or extremities, or a brain or spinal cord injury due to trauma comprising administering to said mammal an effective amount of a pharmaceutical composition comprising (a) a compound having a formula



wherein R^1 is selected from the group consisting of hydrogen, lower alkyl, bridged alkyl, aryl, cycloalkyl, a 4-, 5-, or 6-membered saturated heterocycle, heteroaryl, C_{1-4} alkylenearyl, C_{1-4} alkyleneOaryl, C_{1-4} alkyleneheteroaryl, C_{1-4} alkyleneHet, C_{2-4} alkylenearyl-Oaryl, C_{1-4} alkylene bridged alkyl, C_{1-4} alkylenecycloalkyl, substituted or unsubstituted propargyl, substituted or unsubstituted allyl, and halocycloalkyl;

R^2 is selected from the group consisting of hydrogen, methyl, and halo-substituted methyl;

R^3 is selected from the group consisting of $C(=O)OR^7$, $C(=O)R^7$, $NHC(=O)OR^7$, C_{1-3} alkylene $C(=O)OR^8$, C_{1-3} alkylene $C(=O)R^8$, $C(=NH)NR^8R^9$, $C(=O)NR^8R^9$, $C(=O)C(=O)NR^8R^9$, $C(=O)C(=O)OR^8$, C_{1-4} alkylene OR^8 , aryl, C_{1-3} alkylene-

aryl, C₁₋₃alkyleneheteroaryl, SO₂heteroaryl, Het, and heteroaryl;

R⁴ is selected from the group consisting of hydrogen, lower alkyl, haloalkyl, cycloalkyl, and aryl;

R⁵ is selected from the group consisting of hydrogen, lower alkyl, alkynyl, haloalkyl, hydroxyalkyl, cycloalkyl, and aryl;

R⁶ is selected from the group consisting of hydrogen, lower alkyl, and C(=O)R⁷;

R⁷ is selected from the group consisting of lower alkyl, branched or unbranched, C₁₋₄alkylenearyl, cycloalkyl, Het, C₁₋₄alkylenecycloalkyl, heteroaryl, and aryl, each optionally substituted with one or more of OC(=O)R⁸, C(=O)OR⁸, OR⁸, NR⁸R⁹, or SR⁸;

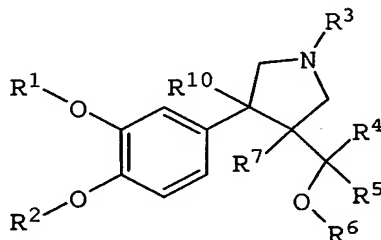
R⁸ and R⁹, same or different, are selected from the group consisting of hydrogen, lower alkyl, cycloalkyl, aryl, heteroaryl, C(=O)Oalkyl, C(=O)Oaryl, C(=O)alkyl, alkylSO₂, haloalkylSO₂, C(=O)C₁₋₃alkylenearyl, C(=O)OC₁₋₄alkylenearyl, C₁₋₄alkylenearyl, and Het, or R⁸ and R⁹ together form a 4-membered to 7-membered ring;

R¹⁰ is selected from the group consisting of hydrogen, alkyl, haloalkyl, cycloalkyl, aryl, C(=O)-alkyl, C(=O)cycloalkyl, C(=O)aryl, C(=O)Oalkyl, C(=O)-Ocycloalkyl, C(=O)aryl, CH₂OH, CH₂Oalkyl, CHO, CN, NO₂, and SO₂R¹¹;

R¹¹ is selected from the group consisting of alkyl, cycloalkyl, trifluoromethyl, aryl, aralkyl, and NR⁸R⁹; or a salt or solvate thereof; and

(b) a pharmaceutically acceptable carrier.

78. (New) A method of treating a mammal for a fibrosis, keloid formation, or scar tissue formation comprising administering to said mammal an effective amount of a pharmaceutical composition comprising (a) a compound having a formula



wherein R¹ is selected from the group consisting of hydrogen, lower alkyl, bridged alkyl, aryl, cycloalkyl, a 4-, 5-, or 6-membered saturated heterocycle, heteroaryl, C₁₋₄alkylenearyl, C₁₋₄alkyleneOaryl, C₁₋₄alkyleneheteroaryl, C₁₋₄alkyleneHet, C₂₋₄alkylenearyl-Oaryl, C₁₋₄alkylene bridged alkyl, C₁₋₄alkylenecycloalkyl, substituted or unsubstituted propargyl, substituted or unsubstituted allyl, and halocycloalkyl;

R² is selected from the group consisting of hydrogen, methyl, and halo-substituted methyl;

R³ is selected from the group consisting of C(=O)OR⁷, C(=O)R⁷, NHC(=O)OR⁷, C₁₋₃alkyleneC(=O)OR⁸, C₁₋₃alkyleneC(=O)R⁸, C(=NH)NR⁸R⁹, C(=O)NR⁸R⁹, C(=O)C(=O)-NR⁸R⁹, C(=O)C(=O)OR⁸, C₁₋₄alkyleneOR⁸, aryl, C₁₋₃alkylenearyl, C₁₋₃alkyleneheteroaryl, SO₂heteroaryl, Het, and heteroaryl;

R⁴ is selected from the group consisting of hydrogen, lower alkyl, haloalkyl, cycloalkyl, and aryl;

R^5 is selected from the group consisting of hydrogen, lower alkyl, alkynyl, haloalkyl, hydroxyalkyl, cycloalkyl, and aryl;

R^6 is selected from the group consisting of hydrogen, lower alkyl, and $C(=O)R^7$;

R^7 is selected from the group consisting of lower alkyl, branched or unbranched, C_{1-4} alkylenearyl, cycloalkyl, Het, C_{1-4} alkylenecycloalkyl, heteroaryl, and aryl, each optionally substituted with one or more of $OC(=O)R^8$, $C(=O)OR^8$, OR^8 , NR^8R^9 , or SR^8 ;

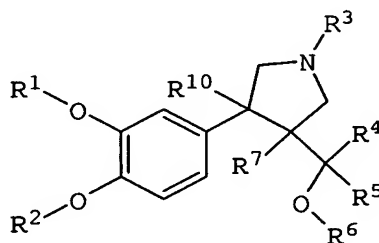
R^8 and R^9 , same or different, are selected from the group consisting of hydrogen, lower alkyl, cycloalkyl, aryl, heteroaryl, $C(=O)Oalkyl$, $C(=O)Oaryl$, $C(=O)alkyl$, $alkylSO_2$, $haloalkylSO_2$, $C(=O)C_{1-3}alkylenearyl$, $C(=O)OC_{1-4}alkylenearyl$, $C_{1-4}alkylenearyl$, and Het, or R^8 and R^9 together form a 4-membered to 7-membered ring;

R^{10} is selected from the group consisting of hydrogen, alkyl, haloalkyl, cycloalkyl, aryl, $C(=O)-alkyl$, $C(=O)cycloalkyl$, $C(=O)aryl$, $C(=O)Oalkyl$, $C(=O)-Ocycloalkyl$, $C(=O)aryl$, CH_2OH , $CH_2Oalkyl$, CHO , CN , NO_2 , and SO_2R^{11} ;

R^{11} is selected from the group consisting of alkyl, cycloalkyl, trifluoromethyl, aryl, aralkyl, and NR^8R^9 ; or a salt or solvate thereof; and

(b) a pharmaceutically acceptable carrier.

79. (New) A method of treating a mammal for systemic lupus erythematosus, a transplant rejection disorder, a graft vs. host reaction, or an allograft rejection comprising administering to said mammal an effective amount of a pharmaceutical composition comprising (a) a compound having a formula



wherein R^1 is selected from the group consisting of hydrogen, lower alkyl, bridged alkyl, aryl, cycloalkyl, a 4-, 5-, or 6-membered saturated heterocycle, heteroaryl, C_{1-4} alkylenearyl, C_{1-4} alkyleneOaryl, C_{1-4} alkyleneheteroaryl, C_{1-4} alkyleneHet, C_{2-4} alkylenearyl-Oaryl, C_{1-4} alkylene bridged alkyl, C_{1-4} alkylenecycloalkyl, substituted or unsubstituted propargyl, substituted or unsubstituted allyl, and halocycloalkyl;

R^2 is selected from the group consisting of hydrogen, methyl, and halo-substituted methyl;

R^3 is selected from the group consisting of $C(=O)OR^7$, $C(=O)R^7$, $NHC(=O)OR^7$, C_{1-3} alkylene $C(=O)OR^8$, C_{1-3} alkylene $C(=O)R^8$, $C(=NH)NR^8R^9$, $C(=O)NR^8R^9$, $C(=O)C(=O)NR^8R^9$, $C(=O)C(=O)OR^8$, C_{1-4} alkylene OR^8 , aryl, C_{1-3} alkylenearyl, C_{1-3} alkyleneheteroaryl, SO_2 heteroaryl, Het, and heteroaryl;

R^4 is selected from the group consisting of hydrogen, lower alkyl, haloalkyl, cycloalkyl, and aryl;

R^5 is selected from the group consisting of hydrogen, lower alkyl, alkynyl, haloalkyl, hydroxyalkyl, cycloalkyl, and aryl;

R^6 is selected from the group consisting of hydrogen, lower alkyl, and $C(=O)R^7$;

R^7 is selected from the group consisting of lower alkyl, branched or unbranched, C_{1-4} alkylenearyl, cycloalkyl, Het, C_{1-4} alkylenecycloalkyl, heteroaryl, and aryl, each optionally substituted with one or more of $OC(=O)R^8$, $C(=O)OR^8$, OR^8 , NR^8R^9 , or SR^8 ;

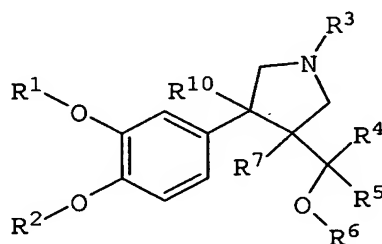
R^8 and R^9 , same or different, are selected from the group consisting of hydrogen, lower alkyl, cycloalkyl, aryl, heteroaryl, $C(=O)Oalkyl$, $C(=O)Oaryl$, $C(=O)alkyl$, $alkylSO_2$, $haloalkylSO_2$, $C(=O)C_{1-3}alkylenearyl$, $C(=O)OC_{1-4}alkylenearyl$, $C_{1-4}alkylenearyl$, and Het, or R^8 and R^9 together form a 4-membered to 7-membered ring;

R^{10} is selected from the group consisting of hydrogen, alkyl, haloalkyl, cycloalkyl, aryl, $C(=O)-alkyl$, $C(=O)cycloalkyl$, $C(=O)aryl$, $C(=O)Oalkyl$, $C(=O)-Ocycloalkyl$, $C(=O)aryl$, CH_2OH , $CH_2Oalkyl$, CHO , CN , NO_2 , and SO_2R^{11} ;

R^{11} is selected from the group consisting of alkyl, cycloalkyl, trifluoromethyl, aryl, aralkyl, and NR^8R^9 ; or a salt or solvate thereof; and

(b) a pharmaceutically acceptable carrier.

80. (New) A method of treating a mammal for chronic glomerulonephritis, nephropathy attributed to Type 2 diabetes, an inflammatory bowel disease, Crohn's disease, or ulcerative colitis comprising administering to said mammal an effective amount of a pharmaceutical composition comprising (a) a compound having a formula



wherein R^1 is selected from the group consisting of hydrogen, lower alkyl, bridged alkyl, aryl, cycloalkyl, a 4-, 5-, or 6-membered saturated heterocycle, heteroaryl, C_{1-4} alkylenearyl, C_{1-4} alkyleneOaryl, C_{1-4} alkyleneheteroaryl, C_{1-4} alkyleneHet, C_{2-4} alkylenearyl-Oaryl, C_{1-4} alkylene bridged alkyl, C_{1-4} alkylenecycloalkyl, substituted or unsubstituted propargyl, substituted or unsubstituted allyl, and halocycloalkyl;

R^2 is selected from the group consisting of hydrogen, methyl, and halo-substituted methyl;

R^3 is selected from the group consisting of $C(=O)OR^7$, $C(=O)R^7$, $NHC(=O)OR^7$, C_{1-3} alkylene $C(=O)OR^8$, C_{1-3} alkylene $C(=O)R^8$, $C(=NH)NR^8R^9$, $C(=O)NR^8R^9$, $C(=O)C(=O)NR^8R^9$, $C(=O)C(=O)OR^8$, C_{1-4} alkylene OR^8 , aryl, C_{1-3} alkylenearyl, C_{1-3} alkyleneheteroaryl, SO_2 heteroaryl, Het, and heteroaryl;

R^4 is selected from the group consisting of hydrogen, lower alkyl, haloalkyl, cycloalkyl, and aryl;

R^5 is selected from the group consisting of hydrogen, lower alkyl, alkynyl, haloalkyl, hydroxyalkyl, cycloalkyl, and aryl;

R^6 is selected from the group consisting of hydrogen, lower alkyl, and $C(=O)R^7$;

R^7 is selected from the group consisting of lower alkyl, branched or unbranched, C_{1-4} alkylenearyl, cycloalkyl, Het, C_{1-4} alkylenecycloalkyl, heteroaryl, and aryl, each optionally substituted with one or more of $OC(=O)R^8$, $C(=O)OR^8$, OR^8 , NR^8R^9 , or SR^8 ;

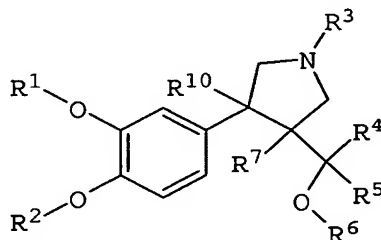
R^8 and R^9 , same or different, are selected from the group consisting of hydrogen, lower alkyl, cycloalkyl, aryl, heteroaryl, $C(=O)Oalkyl$, $C(=O)Oaryl$, $C(=O)alkyl$, $alkylSO_2$, $haloalkylSO_2$, $C(=O)C_{1-3}alkylenearyl$, $C(=O)OC_{1-4}alkylenearyl$, $C_{1-4}alkylenearyl$, and Het, or R^8 and R^9 together form a 4-membered to 7-membered ring;

R^{10} is selected from the group consisting of hydrogen, alkyl, haloalkyl, cycloalkyl, aryl, $C(=O)-alkyl$, $C(=O)cycloalkyl$, $C(=O)aryl$, $C(=O)Oalkyl$, $C(=O)-Ocycloalkyl$, $C(=O)aryl$, CH_2OH , $CH_2Oalkyl$, CHO , CN , NO_2 , and SO_2R^{11} ;

R^{11} is selected from the group consisting of alkyl, cycloalkyl, trifluoromethyl, aryl, aralkyl, and NR^8R^9 ; or a salt or solvate thereof; and

(b) a pharmaceutically acceptable carrier.

81. (New) A method of treating a mammal for proliferative lymphocytic disease or a leukemia comprising administering to said mammal an effective amount of a pharmaceutical composition comprising (a) a compound having a formula



wherein R^1 is selected from the group consisting of hydrogen, lower alkyl, bridged alkyl, aryl, cycloalkyl, a 4-, 5-, or 6-membered saturated heterocycle, heteroaryl, C_{1-4} alkylenearyl, C_{1-4} alkyleneOaryl, C_{1-4} alkyleneheteroaryl, C_{1-4} alkyleneHet, C_{2-4} alkylenearyl-Oaryl, C_{1-4} alkylene bridged alkyl, C_{1-4} alkylenecycloalkyl, substituted or unsubstituted propargyl, substituted or unsubstituted allyl, and halocycloalkyl;

R^2 is selected from the group consisting of hydrogen, methyl, and halo-substituted methyl;

R^3 is selected from the group consisting of $C(=O)OR^7$, $C(=O)R^7$, $NHC(=O)OR^7$, C_{1-3} alkylene $C(=O)OR^8$, C_{1-3} alkylene $C(=O)R^8$, $C(=NH)NR^8R^9$, $C(=O)NR^8R^9$, $C(=O)C(=O)NR^8R^9$, $C(=O)C(=O)OR^8$, C_{1-4} alkylene OR^8 , aryl, C_{1-3} alkylenearyl, C_{1-3} alkyleneheteroaryl, SO_2 heteroaryl, Het, and heteroaryl;

R^4 is selected from the group consisting of hydrogen, lower alkyl, haloalkyl, cycloalkyl, and aryl;

R^5 is selected from the group consisting of hydrogen, lower alkyl, alkynyl, haloalkyl, hydroxyalkyl, cycloalkyl, and aryl;

R^6 is selected from the group consisting of hydrogen, lower alkyl, and $C(=O)R^7$;

R^7 is selected from the group consisting of lower alkyl, branched or unbranched, C_{1-4} alkylenearyl, cycloalkyl, Het, C_{1-4} alkylenecycloalkyl, heteroaryl, and aryl, each optionally substituted with one or more of $OC(=O)R^8$, $C(=O)OR^8$, OR^8 , NR^8R^9 , or SR^8 ;

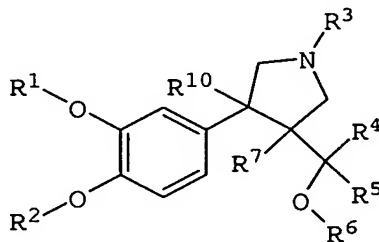
R^8 and R^9 , same or different, are selected from the group consisting of hydrogen, lower alkyl, cycloalkyl, aryl, heteroaryl, $C(=O)Oalkyl$, $C(=O)Oaryl$, $C(=O)alkyl$, $alkylSO_2$, $haloalkylSO_2$, $C(=O)C_{1-3}alkylenearyl$, $C(=O)OC_{1-4}alkylenearyl$, $C_{1-4}alkylenearyl$, and Het, or R^8 and R^9 together form a 4-membered to 7-membered ring;

R^{10} is selected from the group consisting of hydrogen, alkyl, haloalkyl, cycloalkyl, aryl, $C(=O)-alkyl$, $C(=O)cycloalkyl$, $C(=O)aryl$, $C(=O)Oalkyl$, $C(=O)-Ocycloalkyl$, $C(=O)aryl$, CH_2OH , $CH_2Oalkyl$, CHO , CN , NO_2 , and SO_2R^{11} ;

R^{11} is selected from the group consisting of alkyl, cycloalkyl, trifluoromethyl, aryl, aralkyl, and NR^8R^9 ; or a salt or solvate thereof; and

(b) a pharmaceutically acceptable carrier.

82. (New) A method of treating a mammal for an inflammatory dermatosis, atopic dermatitis, psoriasis, or urticaria comprising administering to said mammal an effective amount of a pharmaceutical composition comprising (a) a compound having a formula



wherein R¹ is selected from the group consisting of hydrogen, lower alkyl, bridged alkyl, aryl, cycloalkyl, a 4-, 5-, or 6-membered saturated heterocycle, heteroaryl, C₁₋₄alkylenearyl, C₁₋₄alkyleneOaryl, C₁₋₄alkyleneheteroaryl, C₁₋₄alkyleneHet, C₂₋₄alkylenearyl-Oaryl, C₁₋₄alkylene bridged alkyl, C₁₋₄alkylenecycloalkyl, substituted or unsubstituted propargyl, substituted or unsubstituted allyl, and halocycloalkyl;

R² is selected from the group consisting of hydrogen, methyl, and halo-substituted methyl;

R³ is selected from the group consisting of C(=O)OR⁷, C(=O)R⁷, NHC(=O)OR⁷, C₁₋₃alkyleneC(=O)OR⁸, C₁₋₃alkyleneC(=O)R⁸, C(=NH)NR⁸R⁹, C(=O)NR⁸R⁹, C(=O)C(=O)NR⁸R⁹, C(=O)C(=O)OR⁸, C₁₋₄alkyleneOR⁸, aryl, C₁₋₃alkylenearyl, C₁₋₃alkyleneheteroaryl, SO₂heteroaryl, Het, and heteroaryl;

R⁴ is selected from the group consisting of hydrogen, lower alkyl, haloalkyl, cycloalkyl, and aryl;

R^5 is selected from the group consisting of hydrogen, lower alkyl, alkynyl, haloalkyl, hydroxyalkyl, cycloalkyl, and aryl;

R^6 is selected from the group consisting of hydrogen, lower alkyl, and $C(=O)R^7$;

R^7 is selected from the group consisting of lower alkyl, branched or unbranched, C_{1-4} alkylenearyl, cycloalkyl, Het, C_{1-4} alkylenecycloalkyl, heteroaryl, and aryl, each optionally substituted with one or more of $OC(=O)R^8$, $C(=O)OR^8$, OR^8 , NR^8R^9 , or SR^8 ;

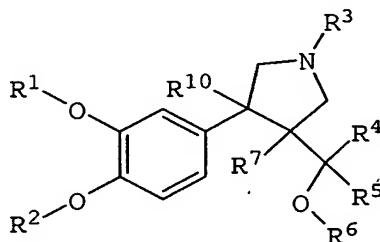
R^8 and R^9 , same or different, are selected from the group consisting of hydrogen, lower alkyl, cycloalkyl, aryl, heteroaryl, $C(=O)Oalkyl$, $C(=O)Oaryl$, $C(=O)alkyl$, $alkylSO_2$, $haloalkylSO_2$, $C(=O)C_{1-3}alkylenearyl$, $C(=O)OC_{1-4}alkylenearyl$, $C_{1-4}alkylenearyl$, and Het, or R^8 and R^9 together form a 4-membered to 7-membered ring;

R^{10} is selected from the group consisting of hydrogen, alkyl, haloalkyl, cycloalkyl, aryl, $C(=O)-alkyl$, $C(=O)cycloalkyl$, $C(=O)aryl$, $C(=O)Oalkyl$, $C(=O)-Ocycloalkyl$, $C(=O)aryl$, CH_2OH , $CH_2Oalkyl$, CHO , CN , NO_2 , and SO_2R^{11} ;

R^{11} is selected from the group consisting of alkyl, cycloalkyl, trifluoromethyl, aryl, aralkyl, and NR^8R^9 ; or a salt or solvate thereof; and

(b) a pharmaceutically acceptable carrier.

83. (New) A method of treating a mammal for a cardiomyopathy, congestive heart failure, atherosclerosis, pyrexia, cachexia, cachexia secondary to infection or malignancy, cachexia secondary to acquired immune deficiency syndrome, ARC, cerebral malaria, osteoporosis, a bone resorption disease, fever and myalgias due to infection, erectile dysfunction, male or female infertility, diabetes insipidus, a central nervous system disorder, an anxiety or stress response, cerebral ischemia, tardive dyskinesia, Parkinson's Disease, or premenstrual syndrome comprising administering to said mammal an effective amount of a pharmaceutical composition comprising (a) a compound having a formula



wherein R^1 is selected from the group consisting of hydrogen, lower alkyl, bridged alkyl, aryl, cycloalkyl, a 4-, 5-, or 6-membered saturated heterocycle, heteroaryl, C_{1-4} alkylenearyl, C_{1-4} alkyleneOaryl, C_{1-4} alkyleneheteroaryl, C_{1-4} alkyleneHet, C_{2-4} alkylenearyl-Oaryl, C_{1-4} alkylene bridged alkyl, C_{1-4} alkylenecycloalkyl, substituted or unsubstituted propargyl, substituted or unsubstituted allyl, and halocycloalkyl;

R^2 is selected from the group consisting of hydrogen, methyl, and halo-substituted methyl;

R^3 is selected from the group consisting of $C(=O)OR^7$, $C(=O)R^7$, $NHC(=O)OR^7$, $C_{1-3}alkyleneC(=O)OR^8$, $C_{1-3}alkyleneC(=O)R^8$, $C(=NH)NR^8R^9$, $C(=O)NR^8R^9$, $C(=O)C(=O)NR^8R^9$, $C(=O)C(=O)OR^8$, $C_{1-4}alkyleneOR^8$, aryl, $C_{1-3}alkylene$ -aryl, $C_{1-3}alkyleneheteroaryl$, $SO_2heteroaryl$, Het, and heteroaryl;

R^4 is selected from the group consisting of hydrogen, lower alkyl, haloalkyl, cycloalkyl, and aryl;

R^5 is selected from the group consisting of hydrogen, lower alkyl, alkynyl, haloalkyl, hydroxyalkyl, cycloalkyl, and aryl;

R^6 is selected from the group consisting of hydrogen, lower alkyl, and $C(=O)R^7$;

R^7 is selected from the group consisting of lower alkyl, branched or unbranched, $C_{1-4}alkylenearyl$, cycloalkyl, Het, $C_{1-4}alkylenecycloalkyl$, heteroaryl, and aryl, each optionally substituted with one or more of $OC(=O)R^8$, $C(=O)OR^8$, OR^8 , NR^8R^9 , or SR^8 ;

R^8 and R^9 , same or different, are selected from the group consisting of hydrogen, lower alkyl, cycloalkyl, aryl, heteroaryl, $C(=O)Oalkyl$, $C(=O)Oaryl$, $C(=O)alkyl$, $alkylSO_2$, $haloalkylSO_2$, $C(=O)C_{1-3}alkylene$ -aryl, $C(=O)OC_{1-4}alkylenearyl$, $C_{1-4}alkylenearyl$, and Het, or R^8 and R^9 together form a 4-membered to 7-membered ring;

R^{10} is selected from the group consisting of hydrogen, alkyl, haloalkyl, cycloalkyl, aryl, $C(=O)$ -alkyl, $C(=O)cycloalkyl$, $C(=O)aryl$, $C(=O)Oalkyl$, $C(=O)O$ -cycloalkyl, $C(=O)aryl$, CH_2OH , $CH_2Oalkyl$, CHO , CN , NO_2 , and SO_2R^{11} ;

R^{11} is selected from the group consisting of alkyl, cycloalkyl, trifluoromethyl, aryl, aralkyl, and NR^8R^9 ; or a salt or solvate thereof; and

(b) a pharmaceutically acceptable carrier.